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Allergen immunotherapy: current and new therapeutic strategies.

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Allergic individuals respond to an environmental allergen encounter by producing T-cell cytokines, predominantly IL-4 and IL-5, which in turn drive the production of allergen-specific IgE antibodies and recruitment of an eosinophil-rich inflammatory infiltrate. Allergen-specific immunotherapy (SIT) involves the repeated injection of the allergen to specifically downregulate this predominantly Th2-type immune response. SIT is a clinically proven effective treatment for allergic diseases, including rhinoconjunctivitis and asthma. However, despite having been in clinical practice since early this century, its use remains empirical. Best practice protocols are based on clinical experience and include recommendations for selecting patients for treatment, SIT regimes and avoidance of adverse events. More rational and safer SIT regimes will result from new insights into the underlying immune mechanisms for allergic disease, in particular the critical role of helper T-cells in orchestrating this response. The development of recombinant techniques for producing purified allergens and allergen derivatives has led to a dramatic improvement in the ability to standardise allergen preparations and to develop novel vaccines for allergy treatment. Potential vaccines include short peptides based on dominant T-cell epitopes of allergens, allergen fragments and mutant allergens. All of these preparations are designed to target T-cells without binding IgE and inducing local and systemic side effects. Additional strategies under consideration include DNA vaccines and fusion protein constructs incorporating immunomodulatory elements such as bacterial cell proteins, cytokines and immunostimulatory sequences of DNA. Different forms of allergens are being evaluated for the more practical mucosal administration of allergy vaccines. The identification of recombinant allergens suitable for diagnostic use and the development of reliable laboratory assays, based on T-cell function to monitor clinical efficacy of SIT, are important practical outcomes from this research.

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